Translation

PATENT COOPERATION TREATY

PCT/JP2003/015201

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P033P01/PCT	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/JP2003/015201	International filing date (*day/month/year*) 27 November 2003 (27.11.2003)	Priority date (*day/month/year*) 28 November 2002 (28.11.2002)
International Patent Classification (IPC) or national classification and IPC A61K 38/00, A61P 9/00, 9/10, 43/00		
Applicant JAPAN SCIENCE AND TECHNOLOGY AGENCY		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

3. This report is also accompanied by ANNEXES, comprising:

   a. ☒ *(sent to the applicant and to the International Bureau)* a total of 1 sheets, as follows:

      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).

      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

   ☒ Box No. I Basis of the report
   ☐ Box No. II Priority
   ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   ☐ Box No. IV Lack of unity of invention
   ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   ☐ Box No. VI Certain documents cited
   ☐ Box No. VII Certain defects in the international application
   ☐ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
24 March 2004 (24.03.2004)	20 December 2004 (20.12.2004)
Name and mailing address of the IPEA/JP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/JP2003/015201

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is language of a translation furnished for the purpose of:

☐ international search (under Rules 12.3 and 23.1(b))

☐ publication of the international application (under Rule 12.4)

☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☐ The international application as originally filed/furnished

☒ the description:

pages 1-30, as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☒ the claims:

pages 1-14, as originally filed/furnished

pages* _____, as amended (together with any statement) under Article 19

pages* 15 received by this Authority on 13 September 2004 (13.09.2004)

pages* _____ received by this Authority on _____

☒ the drawings:

pages 1-9, as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/JP03/15201

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 1-6

because:

☒ the said international application, or the said claims Nos. 1-6 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

The subject matters of claims 1-6 relate to methods for treatment of the human body by therapy.

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 1-6 .

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ see Supplemental Box for further details.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No. PCT/JP03/15201

Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	7-15	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	7-15	NO
Industrial applicability (IA)	Claims	7-15	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Document 1: Recovery from Persistent Glial Cell Swelling under Lactacidosis by Introduction of Anion Channels, (T. Nabekura, et al.), Japanese Journal of Physiology, 2001, Vol. 51, Suppl. S127
Document 2: Co-existence of Necrosis and Apoptosis in Rat Hippocampus Following Transient Forebrain Ischemia, (Yuan-Shan Zeng, et al.), Neuroscience Research, 2000, Vol. 37, No. 2, pages 113-125
Document 3: A Synthetic Peptide Based on a Glycinegated Chloride Channel Induces a Novel Chloride Conductance in Isolated Epithelial Cells, (Kathy E. Mitchell, et al.), Biochimica et Biophysica Acta, 2000, Vol. 1466, pages 47-60

Inventive step
Claims 7-11 and 13-15

Document 1 describes that, in glial cells, RVD is inhibited by lactacidosis and those cells have swelling, but administering VacA so that anion channels form on the membrane makes the said swelling last only for a limited time even under the lactacidosis condition.

Document 2 (page 114, left column) describes that cranial nerve cells have swelling by means of ischemia and such cells die by necrosis.

In respect of the foregoing, the applicant mainly claims in a written reply dated 13 September 2004 (1) that document 1 does not disclose the reduction of necrosis of cells, and (2) that document 2 concerns hippocampus neurons but contains no description of glial cells.

However, document 2 describes that cells may die because of the swelling, and so a person skilled in the art could have easily conceived of using VacA in order to inhibit the swelling of glial cells described in document 1 that is found to lead to the death of cells.

It is considered that the effects of the subject matters of claims 7-11 and 13-15 of the present application are merely predictable from documents 1 and 2 for a person skilled in the art.

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: V

Claims 7-10 and 12-14

Document 3 describes that glycine receptor channel mutant peptides form anion channels on the membrane, whereby they have an effect of increasing anion permeability (page 47, Abstract).

In this respect, the applicant claims in the said written reply (1) that document 3 only describes that glycine receptor channel mutant peptides form anion channels on the epithelial cell membrane but does not describe that the said peptides form anion channels on glial cells and cause the outflow of anions from the cells that leads to RVD, and (2) that, if anion channels are formed on the membrane, the direction of movement of anions depends upon the potential difference and the difference in the anion concentration between the inside and outside of a cell, so it could not have been predicted from document 3 that glycine receptor channel mutant peptides have an effect of inhibiting the death of cells.

However, document 1 describes that forming anion channels on the membrane of swollen glial cells causes the outflow of anions from the cells, and so it is considered that using glycine receptor channel mutant peptides described in document 3 under the same conditions causes the outflow of anions from the cells, as in the above.

Accordingly, even considering such claim, it is not considered that specifying channel proteins produces a particular effect that could not have been predicted from documents 1-3 by a person skilled in the art.